

REMARKS

In response to the Office Action dated September 17, 2009, Applicants provide the following remarks, which are not to be construed as acquiescence with regard to the Examiner's rejections and are made without prejudice to prosecution of any subject matter in a related divisional, continuation or continuation-in-part application. Claims 1-64 are pending and under examination in the application. Favorable reconsideration of the subject application is respectfully requested in view of the following remarks.

CLAIM REJECTIONS UNDER 35 U.S.C. § 103(A)

Claims 1-64 stand rejected under 35 U.S.C. § 103(a), as allegedly being unpatentable over Singh (U.S. Patent Application No. 2002/0197649). Specifically, the Action alleges that it would have been obvious to one of ordinary skill in the art to arrive at the present conjugates because Singh teaches the presently claimed conjugates comprising: 1) a fluorophore or photosensitizer (chlorin); 2) a quenching agent (β -carotene/carotenoid); and 3) a targeting moiety (antibody) for the same rationale as Applicants; namely, using a quenching agent to optimize the photosensitizer before activation.

Applicants respectfully traverse this basis for rejection and submit that the Action fails to provide a sufficient rationale for one having ordinary skill in the art to predictably arrive at the presently claimed invention with any reasonable expectation of success.

To establish a *prima facie* case of obviousness, the Examiner must, at a minimum, show that the cited references teach or suggest all the claim features. See *In re Mayne*, 104 F.3d 1339, 1341-43, 41 U.S.P.Q.2d 1451 (Fed. Cir. 1997) (The PTO has the burden of showing a *prima facie* case of obviousness.). Assuming, *arguendo*, that the cited references teach each claim feature, the Examiner must provide an explicit, apparent reason why a person having ordinary skill in the art would have combined these features in the manner claimed by the Applicants with a reasonable expectation of success. See *KSR v. Teleflex, Inc.*, 237 S. Ct. 1727, 1741 (2007) (“[A] patent composed of several elements is not proved obvious merely by demonstrating that each element was, independently, known in the prior art.”). In the instant

case, the Action has failed to provide sufficient rationale to arrive at the presently claimed conjugates comprising a fluorophore or a photosensitizer, a quenching agent, and a targeting moiety, as claimed.

Applicants respectfully submit that the presently claimed invention is directed, in part, to a conjugate comprising: 1) a fluorophore or a photosensitizer, a quenching agent; and a targeting moiety, wherein: the fluorophore or the photosensitizer is linked to the quenching agent and the targeting moiety in such a way that activation of the fluorophore or the photosensitizer is quenched until the targeting moiety is bound to a target, whereupon the quenching agent moves away from the photosensitizer, enabling activation of the photosensitizer upon irradiation with light of a suitable wavelength; or 2) a tetrapyrrole or tetrapyrrole derivative photosensitizer that comprises a physiologically acceptable metal atom in its central coordination cavity; a quenching agent comprising one or more suitable functional groups that coordinate to the axial position of the metal coordinated within the photosensitizer and position the quenching agent in an energy transfer conformation with the photosensitizer so that activation of the photosensitizer is quenched; and a targeting moiety, wherein binding of the targeting moiety to a target disrupts the association of the axial ligand of the quenching agent to the metal, releasing the quenching agent and rendering the photosensitizer active.

Applicants respectfully submit that while Singh may teach overlapping structural components of the claimed composition, one having skill in the art would recognize that the conjugates of Singh are not structurally identical and are functionally and mechanistically distinct from the presently claimed conjugates. For example, Singh's conjugates require either a single oxygen species from an excited photosensitizer (see Singh, Fig. 1A and B, *e.g.*, element 106; Fig. 2A, B, and E, *e.g.*, PS1) or nuclease (see Singh, Fig. 2C, *e.g.*, element 242; Fig. 2D, *e.g.*, element 258) to cleave the cleavage tags (*e.g.*, Fig. 1A, *e.g.*, cTagk; Fig. 1B, *e.g.*, cTagk; Fig. 2C, *e.g.*, PS-Mk) or a fluorophore or photosensitizer (see Singh, Fig. 2A, B, and E, *e.g.*, PS2; Fig. 2D, *e.g.*, PS-M) to achieve fluorescence. Thus, Singh teaches away from the presently claimed invention, in that, Singh's embodiments **require at least two conjugates or separate molecules** to achieve fluorescence, a photosensitizer (PS1) and photosensitizer/quencher

(PS2/Q) or a nuclease and PS2/Q; whereas, the present invention requires only **a single conjugate** to function.

The Action alleges that Singh teaches conjugates for the same purpose as the presently claimed conjugates, namely to using a quenching agent to optimize the photosensitizer before activation. Applicants respectfully disagree.

One having skill in the art would appreciate that in order to achieve fluorescence, the photosensitizer or fluorophore of Singh **must be cleaved and released** from the conjugate comprising the targeting moiety and the quenching agent, which remain bound to the target tissue. In contrast, the present invention does not involve cleavage of either the fluorophore/photosensitizer or the quenching agent, and in fact, cleavage would render the presently claimed conjugates **inoperable**. In the present invention, the targeting moiety binds to the target tissue and a conformational change in the conjugate increases the distance between fluorophore/photosensitizer and quencher; thus, allowing the fluorophore/photosensitizer to emit fluorescence or produce singlet oxygen species to achieve light therapy. Thus, to remain operable, the presently claimed fluorophore/photosensitizer must remain intact and bound to the target tissue in order for the fluorophore/photosensitizer provide detection of, or light therapy for, the target tissue. Assuming *arguendo*, that one modified the conjugates of Singh so that they lacked cleavage sites, such conjugates would be inoperable because they would always be proximal to the quenching molecule. Thus, Singh teaches away from the presently claimed conjugates, in that, the fluorophore/photosensitizer of Singh must be released from the target site in order to function; whereas, the presently claimed conjugates must remain bound to the target tissues in order for the fluorophore/photosensitizer to remain operable (see, *e.g.*, Figure 1 of the as-filed specification).

Applicants submit that the Action has failed to provide any rationale to provide one having skill in the art with any reasonable expectation of success at arriving at the presently claimed conjugates. Moreover, one having skill in the art would not be motivated to modify the conjugates of Singh and arrive at the presently claimed conjugates with any reasonable expectation of success, because Singh teaches away from the presently claimed conjugates, and such modifications would render the presently claimed conjugates inoperable.

If a proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification. M.P.E.P. § 2143.01, citing *In re Gordon*, 733 F.2d 900 (Fed. Cir. 1984). If there is no motivation to make the proposed modification with a reasonable expectation of success, then there can be no *prima facie* case of obviousness. *KSR v. Teleflex* No. 04-1350 (U.S. Apr. 30, 2007).

Accordingly, Applicants submit that the Action has failed to establish a *prima facie* case of obviousness against the presently claimed invention. Reconsideration and withdrawal of this basis for rejection is respectfully requested.

The Director is authorized to charge any additional fees due by way of this Amendment, or credit any overpayment, to our Deposit Account No. 19-1090.

All of the claims remaining in the application are now believed to be allowable. Favorable consideration and a Notice of Allowance are earnestly solicited.

Respectfully submitted,
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